Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1–44 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is respectfully traversed in view of the above amendments. According to the U.S. Patent and Trademark Office ("PTO"), the claims are overly broad because they are directed to the treatment of all known or yet unknown conditions or disorders associated with α_{2a} or α_{2c} adrenergic receptors. Furthermore, the PTO asserts, based on the data provided in Tables 2 and 4 of the specification, that the yohimbine dimer compounds of the present invention are selective α_{2c} adrenergic receptor antagonists, yet the specification fails to teach a well known utility of α_{2c} adrenergic receptor antagonists or that the α_{2c} adrenergic receptor is responsible for the etiology of any disease condition. Applicants disagree, because the specification does identify conditions mediated by these receptor subtypes. In particular, the specification teaches receptor antagonist activity of the yohimbine dimer compounds at both α_{2a} and α_{2c} adrenergic receptors, and the claims have been amended to include specific diseases associated with α_{2a} or α_{2c} adrenergic receptors. Descriptive support for these amendments appears at page 16, line 16 through page 18, line 22 of the present application. As demonstrated by this portion of the specification, the role of the α_{2a} and α_{2c} receptors in the recited disorders or conditions was known previously. The rejection of claims 1–44 for lack of enablement is, therefore, improper and should be withdrawn.

The rejection of claims 1–23 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments. Since the claims particularly point out what conditions or disorders are being treated, the rejection of claims 1–23 for indefiniteness is improper and should be withdrawn.

The rejection of claims 24–44 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed. According to the PTO, it is not clear whether the activity of the α_{2a} or α_{2c} adrenergic receptor is being inhibited *in vivo* or *in vitro*, nor is it clear how the inhibition is being assessed. Applicants disagree. With respect to how the inhibition is being assessed, Example 5 of the specification teaches measuring *in vitro* antagonism via reversal of medetomidine mediated inhibition of forskolin-induced cAMP levels in α_{2a} or α_{2c} adrenergic receptors. The results confirm that observed binding affinities correlate with the functional response in the α_2 adrenergic receptor subtypes. As to whether

the activity of the α_2 adrenergic receptor subtypes are being inhibited *in vivo* or *in vitro*, persons of skill in the art would expect the observed *in vitro* inhibition to correlate with *in vivo* inhibition. That is, the receptor will be inhibited by the compound regardless of whether the receptor is *in vitro* or *in vivo*. The language is therefore sufficiently clear. For these reasons, the rejection of claims 24–44 for indefiniteness is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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Edwin V. Merkel
Registration No. 40,087

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1128
Facsimile: (585) 263-1600

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Sept. 12, 2005
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Ruth R. Smith
Ruth R. Smith